

Amendments to the Specification

Please amend the specification as follows:

Omit the title on page 1, lines 1-2, and substitute therefor:

**NUCLEIC ACIDS FOR HIGH THROUGHPUT SCREENING OF CpG-BASED
IMMUNO-AGONIST/ANTAGONIST**

Omit the paragraph on page 9, lines 6-18, and substitute therefor:

In a ~~fourth~~ fourth aspect the invention provides isolated nucleic acid molecules which encode full-length murine TLR7. According to this aspect of the invention, isolated nucleic acid molecules are provided which are selected from the group consisting of (a) nucleic acid molecules which hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence set forth as SEQ ID NO:173, and which code for a murine TLR7 having an amino acid sequence set forth as SEQ ID NO:175; (b) nucleic acid molecules that differ from the nucleic acid molecules of (a) in codon sequence due to degeneracy of the genetic code; and (c) complements of (a) or (b). In a certain embodiment, the isolated nucleic acid molecule codes for SEQ ID NO:175, where SEQ ID NO:175 represents the deduced amino acid sequence of full-length murine TLR7. In some embodiments the isolated nucleic acid molecule comprises the nucleotide sequence of SEQ ID NO:173 or SEQ ID NO:174, where these correspond to full-length cDNA and the open reading frame for murine TLR7, respectively.

Omit the paragraph on page 23, lines 1-4, and substitute therefor:

FIG. 10 is a pair of graphs showing amounts of IL-12 induced in (A) human peripheral blood mononuclear cells (PBMC) and (B) murine splenocytes in response to shown concentrations of various ODN, including ODN 2006 (filled circles; SEQ ID NO: 112), 2006-GC (open circles; SEQ ID NO:118), 1668 (filled triangles; SEQ ID NO:84), and 1668-GC (open triangles; SEQ ID NO:85).

Omit the paragraph on page 23, lines 5-9, and substitute therefor:

FIG. 11 is a quartet of graphs depicting responsiveness of 293 cells transfected with hTLR9 (left panels) or mTLR9 (right panels) upon stimulation with shown concentrations of

various ODN, including ODN 2006 (filled circles; SEQ ID NO: 112), 2006-GC (open circles; SEQ ID NO:118), 1668 (filled triangles; SEQ ID NO:84), and 1668-GC (open triangles; SEQ ID NO:85). Responses are shown in terms of induction of NF- κ B-luc (upper panels) and IL-8 (lower panels).

Omit the paragraph on page 23, lines 12-14, and substitute therefor:

FIG. 13 is a pair of graphs showing the responsiveness of (A) 293-hTLR9 and (B) 293-mTLR9 cells to shown concentrations of phosphodiester versions of ODN 2006 (filled circles; SEQ ID NO: 112), 2006-GC (open circles; SEQ ID NO:118), 1668 (filled triangles; SEQ ID NO:84), and 1668-GC (open triangles; SEQ ID NO:85).

Omit the paragraph on page 23, lines 15-16, and substitute therefor:

Fig. 14 is a pair of graphs showing the responsiveness of 293-hTLR9 and 293-mTLR9 cells to shown concentrations of ODN 5002 (filled circles SEQ ID NO:132) and ODN 5007 (open circles; SEQ ID NO:98).

Omit the paragraph on page 23, lines 17-19, and substitute therefor:

FIG. 15 is a bar graph showing the response of 293 cells transfected with mTLR9 to CpG-ODN 1668 (SEQ ID NO:84) is inhibited in a dose-dependent manner by co-exposure to non-CpG-ODN PZ2 (SEQ ID NO:43).

Omit the paragraph on page 24, lines 1-2, and substitute therefor:

FIG. 20 is a bar graph depicting the responsiveness of native form hTLR9 and hTLR9 variant form hTLR9-CXXCm to various stimuli at different concentrations. ODN are as follows: ODN 1668 (SEQ ID NO:84) and ODN 2006 (SEQ ID NO:112).

Omit the paragraph on page 24, lines 3-4, and substitute therefor:

FIG. 21 is a bar graph depicting the responsiveness of native form mTLR9 and mTLR9 variant form mTLR9-CXXCm to various stimuli at different concentrations. ODN are as follows: ODN 1668 (SEQ ID NO:84) and ODN 2006 (SEQ ID NO:112).

Omit the paragraph on page 24, lines 5-7, and substitute therefor:

FIG. 22 is a bar graph showing the responsiveness of native form mTLR9, mTLR9 variant form mTLR9-Phmut, and mTLR9 variant form mTLR9-MBDmut to various stimuli at different concentrations. ODN are as follows: ODN 1668 (SEQ ID NO:84) and ODN 2006 (SEQ ID NO:112).

Omit the paragraph on page 24, lines 8-10, and substitute therefor:

FIG. 23 is a bar graph showing the responsiveness of native form hTLR9, hTLR9 variant form hTLR9-PHmut, and hTLR9 variant form hTLR9-MBDmut to various stimuli at different concentrations. ODN are as follows: ODN 1668 (SEQ ID NO:84) and ODN 2006 (SEQ ID NO:112).

Omit the paragraph on page 24, lines 11-12, and substitute therefor:

FIG. 24 is a bar graph showing the responsiveness of native form mTLR9 and mTLR9 variant form mTLR9-TIRh to various stimuli at different concentrations. ODN are as follows: ODN 1668 (SEQ ID NO:84) and ODN 2006 (SEQ ID NO:112).

Omit the paragraph on page 23, lines 13-14, and substitute therefor:

FIG. 25 is a bar graph showing the responsiveness of native form hTLR9 and hTLR9 variant form hTLR9-TIRm to various stimuli at different concentrations. ODN are as follows: ODN 1668 (SEQ ID NO:84) and ODN 2006 (SEQ ID NO:112).

Omit the paragraph beginning on page 29, line 12, and substitute therefor:

As used herein a murine TLR9 nucleic acid or murine TLR9 polypeptide also embraces homologues and alleles of murine TLR9. In general homologues and alleles typically will share at least 40% nucleotide identity and/or at least 50% amino acid identity to the sequences of specified nucleic acids and polypeptides, respectively. Thus homologues and alleles of murine TLR9 typically will share at least 40% nucleotide identity and/or at least 50% amino acid identity to the sequences of murine TLR9 nucleic acids and TLR9 polypeptides, respectively. In some instances homologues and alleles will share at least 50% nucleotide identity and/or at least 65% amino acid identity and in still other instances will share at least 60% nucleotide identity and/or at least 75% amino acid identity. Preferably the homologues and alleles will share at least

80% nucleotide identity and/or at least 90% amino acid identity, and more preferably will share at least 90% nucleotide identity and/or at least 95% amino acid identity. Most preferably the homologues and alleles will share at least 95% nucleotide identity and/or at least 99% amino acid identity. The homology can be calculated using various publicly available software tools developed by the National Center for Biotechnology Information (NCBI, Bethesda, Maryland) that can be obtained through the internet (~~ftp://ncbi.nlm.nih.gov/pub/~~). Exemplary tools include the BLAST system available from the NCBI at ~~http://www.ncbi.nlm.nih.gov~~, used with default settings. Pairwise and ClustalW alignments (BLOSUM30 matrix setting) as well as Kyte-Doolittle hydrophobic analysis can be obtained, for example, using the MacVector sequence analysis software (Oxford Molecular Group). Watson-Crick complements of the foregoing nucleic acids also are embraced by the invention.